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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/997,267 | 11/30/2001 | Isabelle Ahrens-Fath | SCH-1793 | 2581 |

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| EXAMINER | |
|---|---|
| PAK, MICHAEL D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/997,267 | AHRENS-FATH ET AL. | |
| | Examiner | Art Unit | |
| | Michael Pak | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 July 2005*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-14,16-18,20 and 23-28* is/are pending in the application.

4a) Of the above claim(s) *4-11,16-18,20 and 23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,12-14 and 26-28* is/are rejected.

7)☒ Claim(s) *2 and 3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

1. Amendment filed January 19, 2006 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Applicant's arguments filed January 19, 2006, have been fully considered but they are not found persuasive.

4. New claims 26-28 has been entered. Claims 15, 19, and 21-22 have been cancelled. Claims 1-3, 12-14, and 26-28 are examined below. Claims 24 and 25 are labeled as "previously presented" but appears to be newly submitted claims.

5. Newly submitted claims 24 and 25 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

VIII. Claim 21-22 and 24-25, drawn to a method of using a pharmaceutical agent, classification could not be determined because no structure was provided.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 24-25 are withdrawn from consideration

as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

***Claim Rejections - 35 USC § 112***

6. Claims 1, 12-14 and 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recite hybridizing to complements of SEQ ID NO:2 which is confusing and ambiguous because one skilled in the art do not hybridize nucleic acid to protein of SEQ ID NO:2.

7. Claims 1, 12-14 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection and new matter.

The reason for the rejection has been set forth in the previous office actions.

Claims also encompass nucleic acid which hybridizes to complement of SEQ ID NO:2 which is a polypeptide. One skilled in the art do not hybridize nucleic acid to proteins and is not disclosed in the specification. The claim limitation is new matter not disclosed in the specification.

Claims 1, 12-14 and 26-28 are drawn to a genus of DNAs which encode a genus of androgen receptors that are not defined by any critical or definitive structural limitations because the recitation of "hybridization" language encompass of large genus of nucleic acids which cannot be envisioned by one skilled in the art. The specification only discloses a single species disclosed in Figure 1. Furthermore, page 18 of the specification teaches that androgen does not activate the AR42 or AR32 thus are not androgen receptor in the classical sense (Tilley et al., PNAS, 1989). The specification does not disclose what structural features, other than the full length sequence of the AR42 or AR32, must be retained in order to render a protein as a androgen receptor. The specification fail to disclose what specific functions are considered to be definitive of androgen receptor and what specific structures are critical to their retention. The claims are drawn to a genus that need only be related or retain a function that is "characteristic" of a androgen receptor without a definition of what functions are characteristic and what structures other than the full length sequence of AR42 or AR32 are required for said functions. Without said information, the single species cannot be representative of such a broad genus. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* (*Eli Lilly*) held that a generic claim to human, mammalian or vertebrate protein when only the rat protein sequence was disclosed, did not have written description in the specification. The essential feature of the invention is the single species of DNA encoding the AR42 or AR32. The specification with a single species does not provide support for the claimed genus because *Eli Lilly* held that one skilled in the art could not envision the structure of the genus of proteins in other

species such as human or the genus of mammalian or vertebrate proteins. In the same manner, one skilled in the art cannot envision the genus of andorgen receptors structure and thus the specification does not provide adequate disclosure for the claimed genus.

Applicants argue that the two disclosed species of SEQ ID NO:2 and 4 is sufficient to enable and had possession of the invention. However, as discussed above, the disclosed SEQ ID NO:2 and 4 is not sufficient for one skilled in the art to envision the genus of androgen receptors claimed.

8. Claims 1, 12-14, and 26-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated nucleic acid encoding SEQ ID NO:2 or 4, the isolated vector comprising the above stated nucleic acid, isolated cell comprising the the above stated isolated vector, and the method of expressing nucleic acid in the above stated host cell, does not reasonably provide enablement for the nucleic acid of claims 1(c) and 27-28, the vector of claim 12, the cells and methods of using the cell of claims 13-14 and 26. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The reason for the rejection has been set forth in previous office actions.

The first paragraph of § 112 requires that the patent specification enable "those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech, Inc. v. Novo Nordisk AIS, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27

USPQ2d 1510, 1513 (Fed. Cir. 1993)); see also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). Whether making and using the invention would have required undue experimentation, and thus whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d 731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Likewise, in Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), the court affirmed the holding of invalidity of claims to analogs of the EPO gene under § 112 for lack of enablement where applicants had claimed every possible analog of the EPO gene but had disclosed only how to make EPO and a very few analogs. "[D]espite extensive statements in the specification concerning all analogs of the EPO gene that can be made, there is little enabling disclosure of the particular analogs and how to make them .... There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them

and is therefore not entitled to claim all of them." Id., 927 F.2d at 1213-14, 18 USPQ2d at 1027.

Claims 1-3, 12-14, and 26-28 are too broad to be enabled by a specification that provides only AR42 and AR32 as examples of an embodiment of the claimed invention. Here, independent claims 1 is not limited to DNA encoding any specific androgen receptor from any particular species (e.g., mammal, amphibian, bird or fish). Furthermore, AR42 and AR32 are not androgen receptor in the classical sense that it binds androgen because the specification on page 18 teaches that it does not specifically activates with androgen receptor. The specification only describes one DNA sequence encoding AR42 and AR32 protein member from a large "gene family" from only one species, i.e., human. Claims 12-14 encompass vector or cells using the claims1 which are not enabled for the same reason.

The amount of direction provided in the specification is limited to isolation and characterization of AR42 and AR32 nucleic acid. The specification has identified a range of nucleotides and amino acid of AR42 and AR32, but not which nucleotides and amino acids are critical to binding a androgen ligand and a androgen receptor response element. Neither does the specification identify which amino acid and/or nucleic acid subsequences are conserved between many isotypes, or between species, e.g., mammals, fish, amphibians or birds. Thus, the specification provides no evidentiary basis for reasonably predicting how the primary sequence homology correlates to structural/functional homology. The specification does not teach the critical amino acid/nucleic acid sequences necessary to bind androgen and thereby unmasking the

DBD of the receptor have not been identified. Even proteins with highly homologous sequences can function very differently for example 3-hemoglobin and its gene in normal individuals and patients with sickle cell anemia.

Furthermore, to the extent that the Southern blot/low stringency hybridization analysis described in the specification might suggest the existence of one or more genes encoding other proteins with closely related properties to AR42 or AR32, the specification does not describe the isolation and characterization of these genes or how to make them. Moreover, the fact that other androgen receptors have been isolated, sequenced and characterized in subsequent publications does not lead to the conclusion that the specification taught how to make them. 24 Gould v. Quiaa, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1305 (Fed. Cir. 1987) ("A later dated publication cannot supplement an insufficient disclosure in a prior dated application to render it enabling.") Even the specification describes the hap gene identified by Dejean in 1986 and later identified as being the RAR gene, as giving an "unrelated" pattern under high stringency hybridization analysis.

Assuming arguendo that other DNA sequences were isolated by a low stringency hybridization analysis as described in the specification, whether those DNAs actually encoded androgen receptors or encoded receptors for other ligands appears unpredictable, i.e., a ligand screening assay based on chimeric receptor constructs would have to be performed which would require undue experimentation. As to the state of the art, the modular nature or "domain" organization of nuclear receptor proteins "was first noted in a sequence alignment of the androgen receptors of different species" by

Tilley et al. ( PNAS 1989). Thus, the state of the art appears to be evolving, rather than mature.

Claim 1 limitation (c) encompass hybridizing nucleic acid with a polypeptide of SEQ ID NO:2. One skilled in the art do hybridize nucleic acid with polypeptides (Tilley et al., PNAS, 1989). It would require undue experimentation hybridize nucleic acid with polypeptides.

Therefore, based on the above Wands analysis, a preponderance of the evidence supports a conclusion that one skilled in the art would not have been enabled to make and use the invention of claims without undue experimentation.

***Priority***

9. Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, the applications upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1, 12-14 and 26-28 of this application for the reasons provided above. See MPEP 706.02.

***Claim Rejections - 35 USC § 102***

10. Claims 1, 12-14 and 26-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Zamecnik et al. (WO 97/11170).

Zamecnik et al. disclose a nucleic acid encoding a protein (pages 22-28) which is 98% identical to claimed SEQ ID NO: 2 and vectors, cells comprising the DNA and methods of expressing the DNA (pages 14-15). The claim limitation drawn to

hybridization encompass the nucleic acid of Zamecnik et al. because the nucleic acid Zamecnik et al. has regions of 100% sequence identity which would hybridize. The polypeptide of Zamecnik et al. inherently functions as an androgen binding receptor.

11. Claims 2 and 3 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak, whose telephone number is (571) 272-0879. The examiner can normally be reached on Monday through Friday from 8:30 AM to 2:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Pak

Michael Pak
Primary Patent Examiner
Art Unit 1646
30 March 2006